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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,794	12/20/2000	Ilkka Larma	06267.0053	4230

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EXAMINER	
JOYNES, ROBERT M	
ART UNIT	PAPER NUMBER
1615	16

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,794	LARMA ET AL.	
	Examiner	Art Unit	
	Robert M. Joynes	1615	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of applicants Request for Reconsideration filed on March 17, 2003.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 11, 15 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,531,458. Although the conflicting claims are not identical, they are not

patentably distinct from each other. U.S. Patent No. 6,531,458 claims a pharmaceutical composition comprising levosimendan and alginic acid in the form of tablets, dragees, capsules, powders or granules.

The instant claims are drawn to a controlled release composition for oral administration comprising levosimendan and a drug release-controlling component for providing the release of levosimendan over an extended period of time. The instant claims further recite that the drug release-controlling component can be a hydrophilic gel-forming polymer. Alginic acid falls within that category.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to prepare a pharmaceutical composition comprising levosimendan and alginic acid wherein the composition displays a controlled release profile.

One of ordinary skill in the art would have been motivated to do this to prepare stable dosage forms that achieve the desired release profile for the active agent incorporated in the composition.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 and 8-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haikala et al. (WO 9321921) in view of Frisbee(US 5213811).

Haikala teaches the drug levosimendan as a known an anti-ischemic drug (Page 1, lines 1-29). The drug is a known PDE III inhibitor along with pimobendan and milrinone (Page 1, lines 21-23). These compounds can be formulated into tablets, dragees, capsules, suppositories, emulsions, suspensions or solutions with suitable carriers, solvents, gel forming ingredients, dispersion forming ingredients, antioxidants, colors, sweeteners and wetting agents (Page 1, line 30 – Page 2, line 13).

Frisbee teaches a sustained release drug composition comprising two different release profile compositions (Col. 1, line 61 – Col. 2, line 62). One component is a sustained release composition (Col. 2, lines 19-21) and the second is a rapid release (Col. 2, lines 27-30). The sustained release component comprises a bead on which a coating of the drug, hydroxypropyl methylcellulose and a plasticizer (Col. 1, line 61 – Col. 2, line 21). This component is further coated with a mixture of ethyl cellulose, hydroxypropyl cellulose, polyvinyl acetate phthalate and a plasticizer (Col. 2, lines 8-18). The rapid release component has the same coatings as the sustained release

component but has an additional coating of the drug layer on the outside of the bead or as an end layer (Col. 2, lines 22-26). The active agent of the composition is milrinone (Col. 3, lines 9-21). Frisbee does not expressly teach that the active agent is levosimendan or the exact concentration ranges of the specific components.

While the reference does not teach the complete concentration range, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to combine the teachings of Haikala with those of Frisbee. Haikala teaches a known anti-ischemic drug and other similar drugs. Haikala further teaches that various formulations with known pharmaceutical substances can be made by one of ordinary skill in the art. One of ordinary skill would look to similar drugs, such as the equivalents recited in Haikala for suitable formulation for levosimendan. Frisbee teaches one such formulation with a known anti-ischemic drug wherein two release profiles are achieved.

One of ordinary skill in the art would have been motivated to do this to prepare levosimendan in a sustained release formulation. Again, one would be motivated by the availability of the active agent and by the effectiveness for the desired host.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haikala in view of Frisbee further in view of Yarwood et al(EP 0091767). The teachings of Frisbee and Haikala are discussed above. Neither Frisbee nor Haikala teach the addition of microcrystalline cellulose as an excipient.

Yarwood teaches that microcrystalline cellulose is a known excipients to be used in pharmaceutical formulations.

Whether Yarwood is taken with Frisbee in view of Haikala or Haikala in view of Frisbee, at the time the invention was made, it would have been obvious to a person of ordinary skill in the art to include known excipients such as microcrystalline cellulose in the formulation including levosimendan. Haikala teaches that any suitable components may be included in formulations of levosimendan. Microcrystalline cellulose is a known pharmaceutical component.

One of ordinary skill in the art would have been motivated to do this to add weight to the formulation or add filler to a capsule or tablet.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments with respect to claims 1-17 have been considered but are moot in view of the new ground(s) of rejection.

Applicant's arguments filed March 17, 2003 have been fully considered but they are not persuasive. Applicants argue that no motivation to combine references exists. It is the position of the Examiner that the primary reference teaches the instant drug and teaches that the drug can be in known pharmaceutical formulations such as tablets, dragees, capsules, suppositories, emulsions, suspensions or solutions with suitable carriers, solvents, gel forming ingredients, dispersion forming ingredients, antioxidants, colors, sweeteners and wetting agents, as stated above. The same primary reference recites two equivalent drugs for treating the same condition, pimobendan and milrinone. The secondary references teaches a sustained release composition for one of the known equivalents. It is the position of the Examiner that one of ordinary skill in the art would look to secondary references for compositions comprising equivalent drugs with the same desired effect (i.e., rapid and controlled release) for guidance as to how to prepare formulations for the drug if the primary reference. One would be motivated to do so to achieve the same desired effect for the new drug. Therefore, the Examiner believes there is sufficient motivation to sustain the above rejections.

Conclusion

Due to the new grounds of rejection, this action is deemed non-final.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Joynes whose telephone number is (703) 308-8869. The examiner can normally be reached on Mon.-Thurs. 8:30 - 6:00, alternate Fri. 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Robert M. Joynes
Patent Examiner
Art Unit 1615
May 30, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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